MK5 activates Rag transcription via Foxo1 in developing B cells.

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Public Summary:
Foxo1 is a critical, direct regulator of Rag (recombination activating gene) transcription during B cell development and is thus essential for the generation of a diverse repertoire of antigen receptors. Although Foxo1 regulation has been widely studied in many cell types, pathways regulating Foxo1 in B cells have not been fully elucidated. By screening a panel of Foxo1 mutants, we identified serine 215 on Foxo1 as a novel phosphorylation site that is essential for the activation of Rag transcription. Mutation of S215 strongly attenuated transactivation of Rag but did not affect most other Foxo1 target genes. We show that MK5, a MAPK-activated protein kinase, is a previously unidentified upstream regulator of Foxo1. MK5 was necessary and sufficient to activate Rag transcription in transformed and primary pro-B cells. Together, our experiments show that MK5 positively regulates Rag transcription via phosphorylation of Foxo1 in developing B cells.

Scientific Abstract:
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